Functional connectivity in dementia with Lewy bodies compared to Alzheimer's disease; a network perspective

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1) Introduction

Dementia with Lewy bodies (DLB) is the second to third most common cause of neurodegenerative dementia after Alzheimer's disease (AD). It is characterised by cognitive fluctuations, visual hallucinations, and Parkinsonism. However, at early stages both diseases can present similar clinical phenotypes which obstruct differential diagnosis and proper treatment.

In our research, we study resting state functional magnetic resonance imaging (rs-fMRI) to study the different mechanisms altering the brain and to find biomarkers that help in the differential diagnosis of these neurodegenerative diseases

2) Resting state fMRI

rs-fMRI is a neuroimaging modality were the patient lays awake within the MRI scanner either with eyes open or closed, thinking in nothing in particular.

In the resting state, different brain systems or networks interact as a reflection of the intrinsic connectivity of the brain which previous research has demonstrated is linked to the brain's structural wiring i.e. the physical neuronal connections.

By the study of these networks it is possible to detect brain alterations and insults caused by neurodegenerative diseases and which are not visible from standard MRI.

Figure 1. Newcastle Magnetic Resonance Imaging Centre

3) Brain connectivity in dementia with Lewy bodies and Parkinson's disease dementia

Functional connectivity in DLB is altered compared to a healthy brain. A common finding in DLB is a disconnection between frontal cortex and precuneus cortex as shown in Figure 2. This pattern of disconnection is also found in other dementias such as Alzheimer's disease and it is linked to neuronal loss.

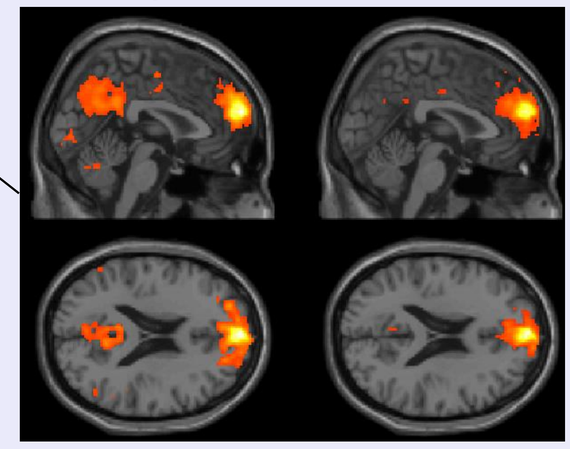


Figure 2. Functional connectivity, seed analysis in frontal cortex

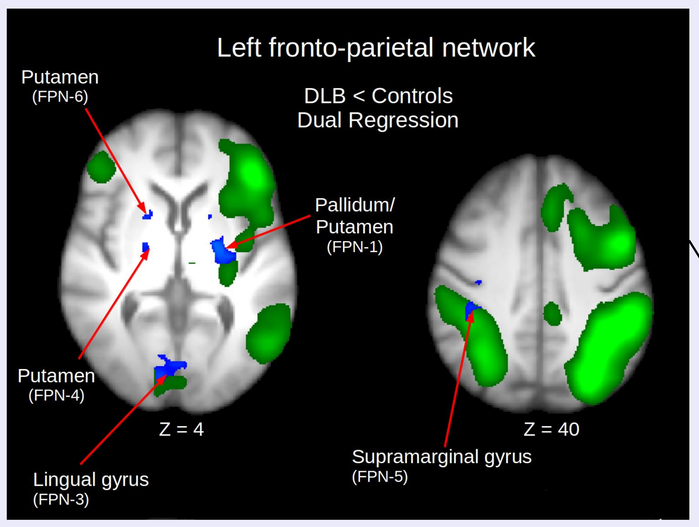


Figure 3. Functional dissociations between the attention network (in green) and several inner brain regions and occipital cortex.

At the level of systems, the brain also suffers alterations caused by DLB. In Figure 3, the fronto-parietal resting state network which is implicated in attention/executive function is shown in green. The blue areas show regions that are disconnected or dissociated from this network in DLB.

Our research indicate that these dissociations are related to cognitive fluctuations in DLB; one of the core clinical features of this disease [1].

Functional alterations also occur subcortically in areas such as the thalamus. This structure which is normally seen as a "switchboard" of information for the brain and it is also implicated as a modulator of attention and arousal, shows more spread connectivity in DLB and PDD.

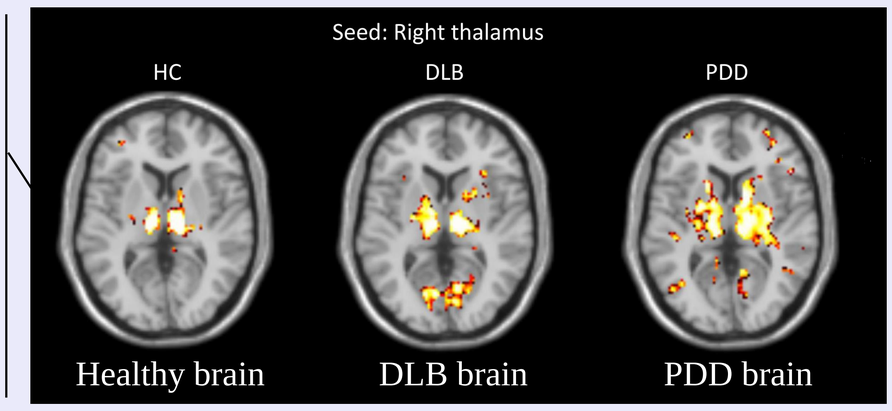
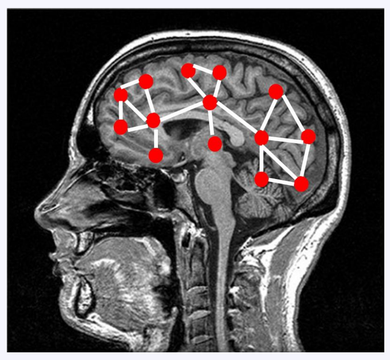


Figure 4. Functional connectivity alterations in DLB, PDD compared to healthy brain. Seed is located at the right thalamus.

4) Brain networks in dementia with Lewy bodies and Alzheimer's disease



Brain's functional connectivity can also be analysed using Graph Theory, which studies the structure and properties of graphs also called networks or webs.

In our research, we use network analysis to study differences between dementias (mainly DLB and Alzheimer's disease) and healthy brain.

We found network differences between DLB and AD patients.

The glass brains at the right show differences between DLB and AD by their nodal clustering coefficient (a measure of local connectivity or communities). Network structure between both diseases is significantly different in temporal cortices (shown as red spheres; AD<DLB) and frontal and parietal cortices (shown as blue spheres; AD>DLB).

Temporal cortical pathology is a common feature in AD. However, clustering co-efficient alterations in parietal and frontal regions in DLB is a new finding that might be related to the distribution of Lewy bodies in this dementia [3].

We also found high positive correlation between global cognitive scores (MMSE and CAMCOG) and global network scores (global efficiency and clustering coefficient) in our DLB cohort. Which is consistent with the concept of better brain connectivity related to better cognitive scores.

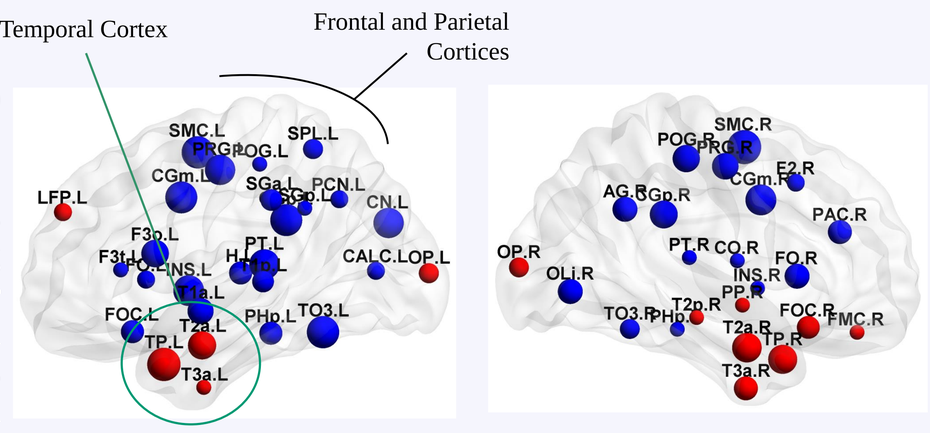


Figure 5. Brain network differences between DLB and AD; clustering coefficient

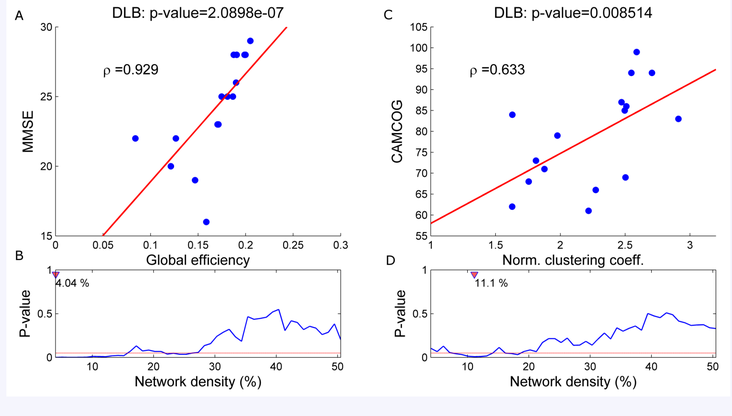


Figure 6. Correlation between global network measures and cognitive scores in DLB

5) Final remarks and more information

Resting state fMRI is a potential tool to study neurodegenerative diseases and explain mechanistic processes as well as have the potential to be a biomarker of disease and symptom severity.

Other neuroimaging modalities can also be applied jointly with functional imaging such as cortical thickness MRI and/or diffusion tensor imaging (DTI). This latter has been used successfully to study brain development and aging [4].

For more information you can visit the Newcastle Institute of Neuroscience webpage: http://www.ncl.ac.uk/ion/

And for brain connectivity also visit:
http://www.dynamic-connectome.org/

Acknowledgments

The research was funded by an Intermediate Clinical Fellowship to Dr J-P. Taylor (WT088441MA) and also supported by Newcastle Biomedical Research Unit (BRU) and the National Institute for Health Research (NIHR). Dr. M. Kaiser was supported by the Human Green Brain Project funded by EPSRC (EP/K026992/1), and CARMEN funded by EPSRC (EP/E002331/1).

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